Supplemental Online Content

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Contents

List of Figures

List of Tables

Systematic literature review and network meta-analysis of ACR response with bDMARDs

A network meta-analysis of randomized controlled trials evaluating bDMARD treatment among bDMARD-naive cDMARD-IR RA patients was performed to obtain American College of Rheumatology 20/50/70 response estimates at the end of a 6-month treatment period. The relevant trials for the network meta-analysis were selected from a larger systematic literature review.

Systematic literature review PICOS selection criteria

Population

- Adult (>18 years) patients with moderate to severe RA who have had inadequate response to cDMARDs

Interventions and comparators

- Biologics as monotherapy or in combination with cDMARDs (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, abatacept, rituximab, tocilizumab, sarilumab, tofacitinib, baricitinib)
- Triple therapy (MTX, HCQ, and SSZ)
- cDMARDs alone or in combination (MTX, HCQ, SSZ or LEF)

Outcomes

- ACR20/ACR50/ACR70
- DAS28
- Total sharp score
- HAQ-DI score
- SF-36 PCS and MCS
- EQ-5D (VAS and utility scores)
- AEs leading to drop-outs

Study design

- Randomized controlled trials

Other

- Studies published in English
- Primary study available as full text published manuscript only; no study available as a conference abstract only was included with the exception of abstracts pertaining to investigational products, baricitinib and sarilumab

Criteria for studies to be selected from the systematic literature review and included in the network meta-analysis

The following criteria were used to select relevant studies to be included in the network meta-analysis of American College of Rheumatology 20/50/70 response estimates at the end of a 6-month treatment period:

Population

- Adult (>18 years) patients with moderate to severe RA who have had inadequate response to cDMARDs and are bDMARD-naive

Interventions

- Biologics as monotherapy or in combination with cDMARDs (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, abatacept, rituximab, tocilizumab, sarilumab, tofacitinib, baricitinib)

Comparators

- cDMARDs
- Any active comparator that allows for an indirect comparison between the bDMARDs of interest

Outcomes

- ACR20/ACR50/ACR70 at 6 months follow-up

Identification and selection of relevant studies

A systematic literature search using MEDLINE, EMBASE, and Cochrane Library databases was performed to identify published randomized controlled trials (January 1990 - August 24, 2016). The search strategy is provided in Supplemental Table 1, Supplemental Table 2, and Supplemental Table 3. Two researchers independently reviewed titles and abstracts of studies identified from the electronic databases to determine eligibility; full texts of potentially relevant studies were then reviewed. In cases of any uncertainty about inclusion of trials, a third researcher was consulted and provided arbitration.

Identified evidence base

Supplemental Figure 1 summarizes the study identification and selection process. Of the 181 studies included in the large systematic literature review, 79 studies concerned the bDMARD-naive population (Supplemental Table 4). There were 66 studies evaluating 36 interventions for which ACR response criteria were reported at 6 months (with a tolerability window of ±4 weeks). The corresponding evidence network is presented in Supplemental Figure 2. For the network meta-analysis the following were deemed to be clinically equivalent and were pooled:

- “INF 3mg/kg q8w” or “INF 5mg/kg q8w” or “INF 6mg/kg q8w”
- “ETN 50mg qw” or “ETN 25mg biw”
- “ABA 10mg/kg q4w” or “ABA SC 125mg qw”
- “CER 200mg q2w+MTX” or “CER 400mg q4w+MTX
- DMARDs including methotrexate, sulfasalazine, hydroxychloroquine, leflunomide at any dosage; studies which only described DMARD therapy as conventional or nonbiologic

Network meta-analysis to obtain ACR 20/50/70 response

The probability of ACR20/50/70 responses was estimated using a Bayesian (random effects) network meta-analyses model for ordered categorical data (Dias et al. 2013). The model assumes that there is an underlying continuous variable (ACR20/50/70) categorized by specifying different cutoffs corresponding to the point at which an individual moves from one category to the next in each trial. The advantage of this approach over an analysis that considers ACR categories separately is that all possible outcomes are analyzed simultaneously based on the same randomized controlled trials, allowing for consistent estimates by category. To avoid influencing the observed results by prior belief, uninformative prior distributions were used for the estimated model parameters. The relative treatment effects for each bDMARD versus cDMARDs estimated on the probit scale were transformed into absolute probabilities of the nonoverlapping ACR response categories by combining them with the average results for cDMARDs. The posterior distributions of parameters of interest were summarized by the median as a reflection of the point estimate and 95% credible intervals, constructed from the 2.5 and 97.5 percentiles. Analyses were performed with the Markov chain Monte Carlo method using the OpenBUGS software package (www.openbugs.net).

Technical details of cost-effectiveness model

Relationship between EULAR Response and ACR Response

We estimated the conditional probability of EULAR response given ACR response using Table 165 from Stevenson et al. (2016). The conditional probabilities in our baseline scenario are show in Supplemental Table 5.

These probabilities were used to simulate EULAR response for a given simulated ACR response. In particular, we simulated EULAR response using a categorical distribution with $k = 3$ categories,

$$eular|acr \sim Cat(3, p_1, p_2, p_3),$$

where for a given ACR response, p_1 is the probability of having no EULAR response, p_2 is the probability of moderate EULAR response, and p_3 is the probability of a good EULAR response.

Simulating treatment duration

To transform the Corrona adjusted BSRBR hazard functions into survival functions, we reconstructed individual patient data using the algorithm described in Guyot et al. (2012). We then estimated parametric survival models for both moderate and good EULAR responders using exponential, Weibull, Gompertz, gamma, log-logistic, and log-normal distributions. We calculated the Akaike information criterion (AIC) and Bayesian information criterion (BIC) for each distribution. For each response type, we selected the log-normal distribution because it had both the lowest AIC and BIC.

In our probabilistic sensitivity analysis (PSA), the parameters of the lognormal survival model were sampled for both moderate and good EULAR responders using the multivariate normal distribution,

$$\theta_i = [\mu_i, \sigma_i] \sim N(\widehat{\theta}_i, \widehat{\Sigma}_i),$$

where $i = m, g$ denotes whether the patient was a moderate or good EULAR responder, μ_i and σ_i are the mean and standard deviation of the lognormal distribution respectively, $\widehat{\theta}_i = [\widehat{\mu}_i, \widehat{\sigma}_i]$ is a vector containing the maximum likelihood estimates of the mean and standard deviation respectively, and $\widehat{\Sigma}_i$ is the maximum likelihood estimate of the variance-covariance matrix. In our patient-level simulation model and for each sample of θ_i, we simulated treatment duration, t, from a lognormal distribution conditional on EULAR response,

$$t \sim LN(\mu_i, \sigma_i).$$

Simulating pain score from simulated HAQ

To simulate pain from HAQ, we used the summary statistics for pain and HAQ reported in Sarzi-Puttini et al. (2002). Pain was measured with the visual analog scale (VAS) with mean $\mu_{pain} = 61.65$ and standard deviation $\sigma_{pain} = 19.10$, while HAQ was reported to have mean $\mu_{haq} = 1.39$ and standard deviation $\sigma_{haq} = 0.59$.

We then estimated the correlation between pain and HAQ by digitally scanning the curve depicting the (linear) relationship between pain and HAQ (Figure 114) shown in Stevenson et al. (2016). Using the scanned data, we regressed pain on HAQ using simple ordinary least squares (OLS). The correlation between pain and HAQ, estimated as $\rho = 0.52$, was calculated by rearranging the OLS estimate for the slope, β, of the regression model,

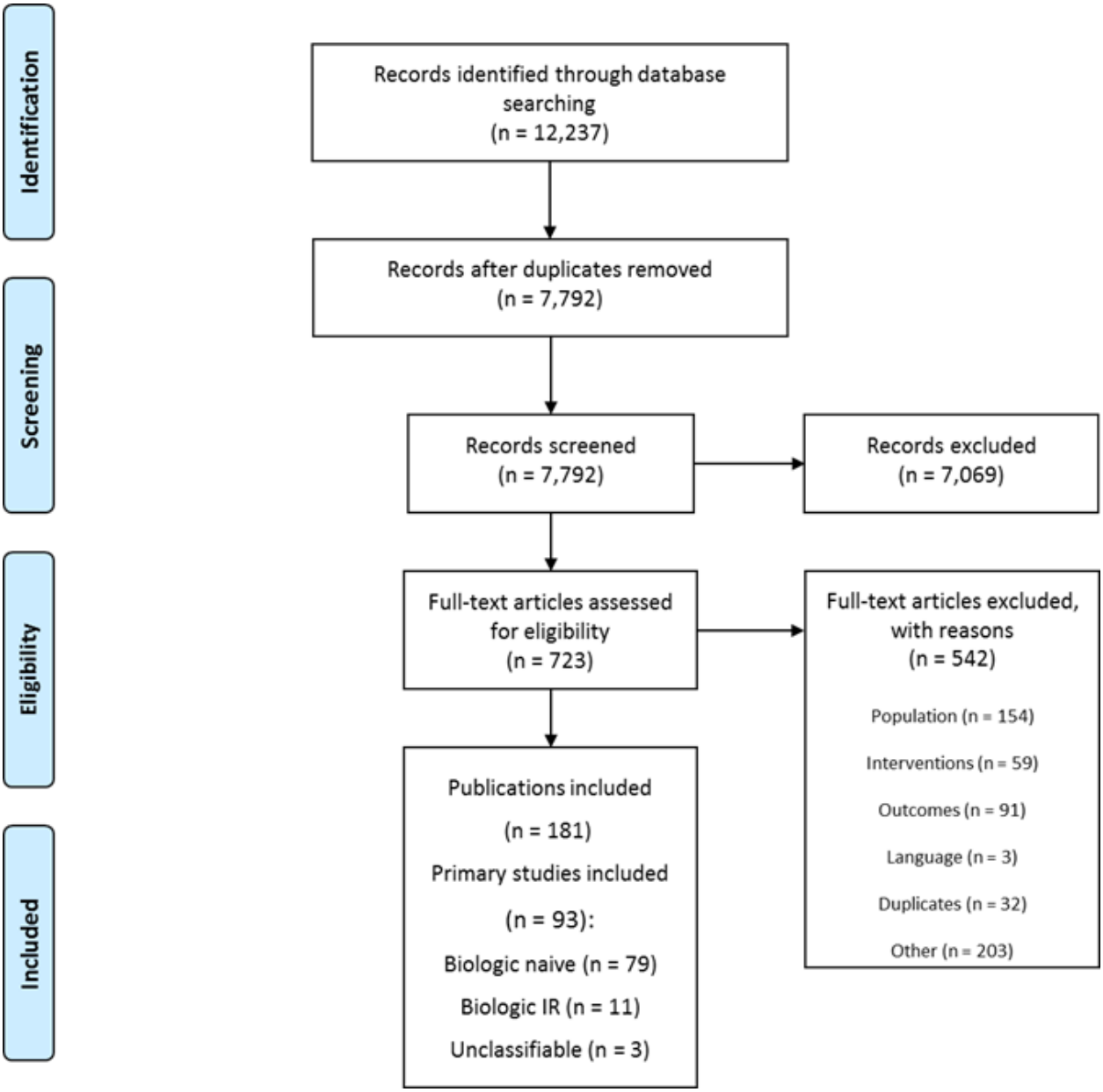
$$\rho = \beta * \frac{\sigma_{haq}}{\sigma_{pain}}.$$

Pain was simulated using these parameters by assuming that pain was normally distributed conditional on HAQ,

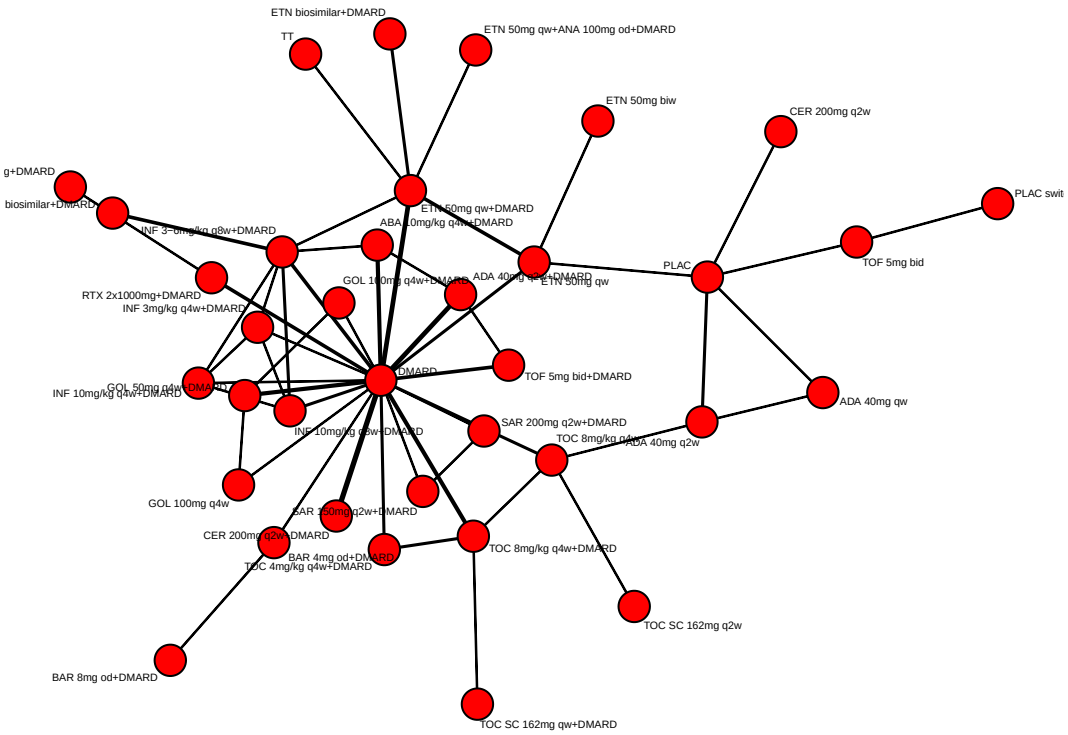
$$pain|haq = h \sim N\left(\mu_{pain} + \rho\frac{\sigma_{pain}}{\sigma_{haq}}(h - \mu_{haq}), \sigma^2_{pain}(1 - \rho^2)\right).$$

However, since the VAS is constrained to lie between 0 and 100, pain was drawn from a truncated normal distribution with a lower limit of 0 and an upper limit of 100.

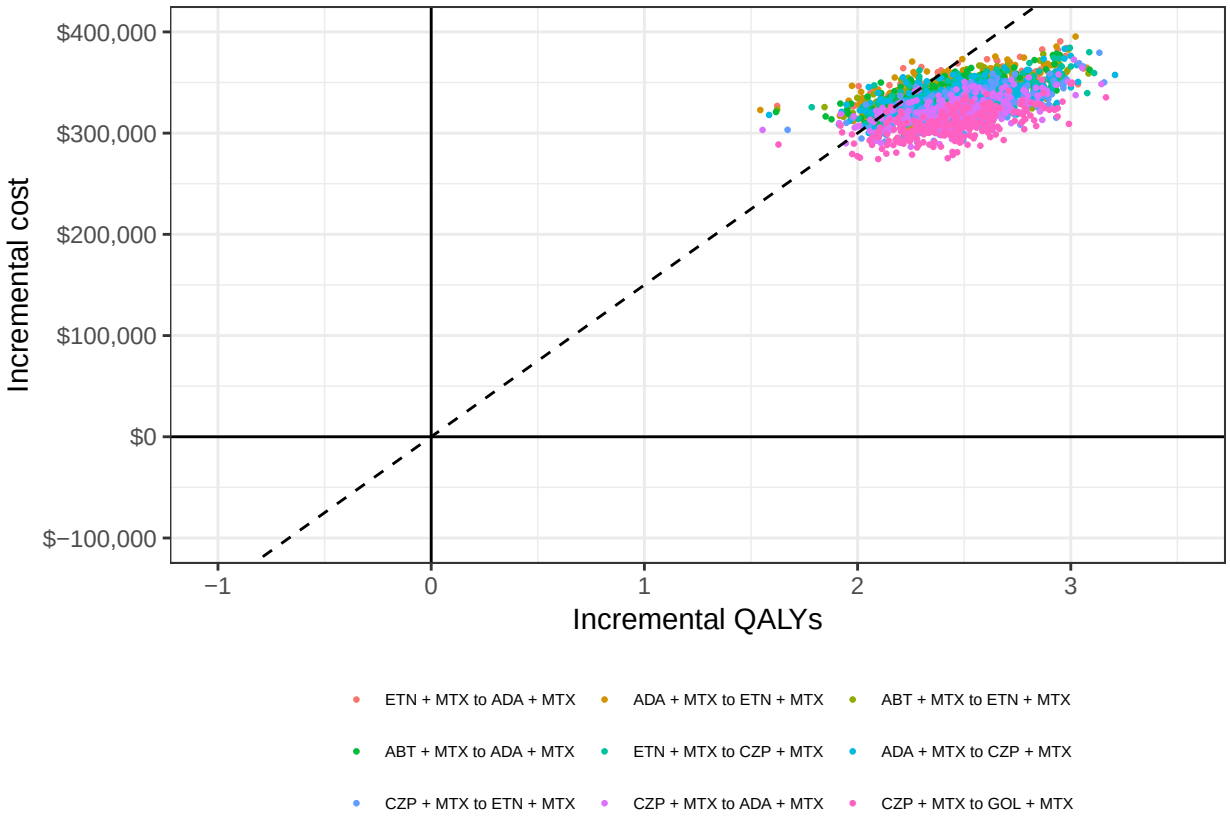
Supplemental Figures



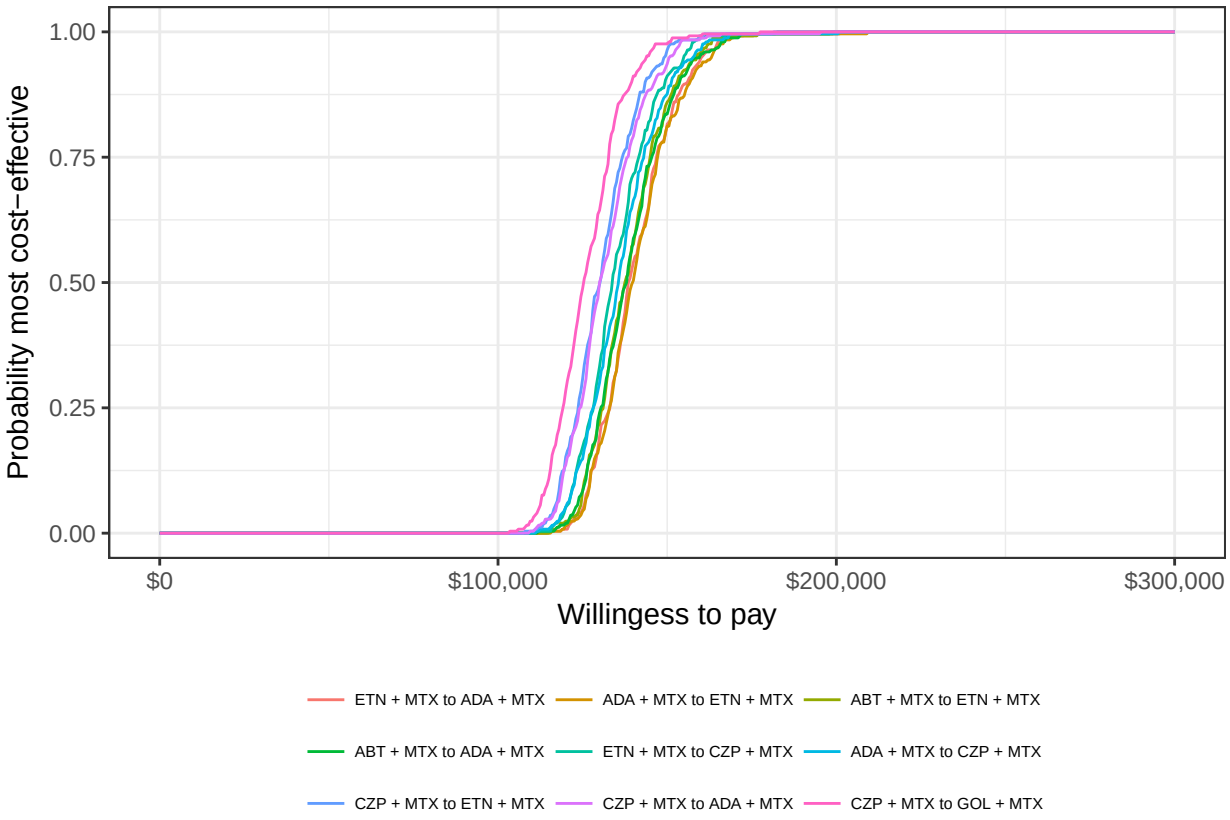
Supplemental Figure 1: Study identification and selection



Supplemental Figure 2: Bayesian random effects NMA network diagram for patients naive to bDMARDs



Supplemental Figure 3: Cost-effectiveness plane with incremental cost and QALY estimates for bDMARD sequences relative to conventional DMARDs under base-case scenario. The dashed line denotes a willingess to pay of $150,000 per QALY.



Supplemental Figure 4: Cost-effectiveness acceptability curves for bDMARD sequences relative to conventional DMARDs under base-case scenario

Supplemental Tables

Supplemental Table 1: EMBASE literature search strategy

Search term	Hits
1. exp rheumatoid arthritis/	172,644
2. *caplans syndrome/	5,932
3. *feltys syndrome/	562
4. *rheumatoid nodule/	659
5. *sjogrens syndrome/	7,178
6. *stills disease,adult-onset/	495
7. (felty$ adj2 syndrome).tw.	797
8. (caplan$ adj2 syndrome).tw.	150
9. (rheumatoid adj nodule).tw.	301
10. (sjogren$ adj2 syndrome).tw.	16,217
11. still$ disease.tw.	2,529
12. (arthritis adj2 rheumat$).tw.	126,307
13. methotrexate.tw.	51,865
14. mexate.tw.	66
15. amethopterin$.tw.	560
16. trexall.tw.	58
17. rheumatrex.tw.	192
18. adalimumab.tw.	10,441
19. humira.tw.	2,568
20. infliximab.tw.	17,558
21. remicade.tw.	4,089
22. etanercept.tw.	10,155
23. enbrel.tw.	3,173
24. certolizumab.tw.	1,830
25. cimzia.tw.	618
26. golimumab.tw.	1,793
27. simponi.tw.	377
28. sulfasalazine.tw.	4,095
29. salazosulfapyridine.tw.	353
30. azulfidine.tw.	680
31. sulfazine.tw.	8
32. salazopyrin.tw.	590
33. hydroxychloroquine.tw.	4,573
34. plaquenil.tw.	1,107
35. anakinra.tw.	2,537
36. kineret.tw.	815
37. abatacept.tw.	2,494

Continued on next page

Supplemental Table 1: EMBASE literature search strategy

Search term	Hits
38. orencia.tw.	540
39. rituximab.tw.	28,986
40. mabthera.tw.	1,905
41. rituxan.tw.	2,785
42. tofacitinib.tw.	801
43. xeljanz.tw.	75
44. jakvinus.tw.	3
45. tocilizumab.tw.	3,604
46. actemra.tw.	381
47. baricitinib.tw.	85
48. LY3009104.tw.	18
49. sarilumab.tw.	52
50. SAR153191.tw.	1
51. REGN88.tw.	4
52. clinical trial/	867,091
53. Randomized controlled trial/	416,927
54. randomization/	71,561
55. single blind procedure/	22,839
56. double blind procedure/	133,477
57. crossover procedure/	48,390
58. placebo/	292,471
59. randomi?ed controlled trial$.tw.	142,434
60. rct.tw.	21,338
61. random allocation.tw.	1,597
62. randomly allocated.tw.	25,734
63. allocated randomly.tw.	2,172
64. (allocated adj2 random).tw.	843
65. single blind$.tw.	18,153
66. double blind$.tw.	171,556
67. ((treble or triple) adj blind$).tw.	607
68. placebo$.tw.	243,378
69. prospective study/	348,476
70. 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69	1,628,384
71. case study/	39,726
72. case report.tw.	322,164
73. abstract report/ or letter/	989,876
74. 71 or 72 or 73	1,344,519
75. 70 not 74	1,586,310
76. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 11 or 12	202,073

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Supplemental Table 1: EMBASE literature search strategy

Search term	Hits
77. or/13-51	119,822
78. 75 and 76 and 77	7,143
79. limit 78 to (english language and yr="1990 -Current")	6,538

Supplemental Table 2: MEDLINE literature search strategy

Search term	Hits
1. exp rheumatoid arthritis/	101,213
2. *Caplan Syndrome/	132
3. *Felty Syndrome/	535
4. *Rheumatoid Nodule/	597
5. *Sjogren's Syndrome/	8,696
6. *Still's Disease, Adult-Onset/	1,001
7. (felty$ adj2 syndrome).tw.	701
8. (caplan$ adj2 syndrome).tw.	116
9. (rheumatoid adj nodule).tw.	248
10. (sjogren$ adj2 syndrome).tw.	12,849
11. still$ disease.tw.	1,875
12. (arthritis adj2 rheumat$).tw.	89,929
13. methotrexate.tw.	35,316
14. mexate.tw.	1
15. amethopterin$.tw.	415
16. trexall.tw.	1
17. rheumatrex.tw.	3
18. adalimumab.tw.	4,316
19. humira.tw.	149
20. infliximab.tw.	9,168
21. remicade.tw.	256
22. etanercept.tw.	5,358
23. enbrel.tw.	241
24. certolizumab.tw.	627
25. cimzia.tw.	21
26. golimumab.tw.	551
27. simponi.tw.	14
28. sulfasalazine.tw.	2,758
29. salazosulfapyridine.tw.	231
30. azulfidine.tw.	74
31. sulfazine.tw.	3
32. salazopyrin.tw.	153
33. hydroxychloroquine.tw.	2,692
34. plaquenil.tw.	112
35. anakinra.tw.	1,145
36. kineret.tw.	70
37. abatacept.tw.	968
38. orencia.tw.	29
39. rituximab.tw.	14,579

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Supplemental Table 2: MEDLINE literature search strategy

Search term	Hits
40. mabthera.tw.	148
41. rituxan.tw.	243
42. tofacitinib.tw.	354
43. xeljanz.tw.	10
44. jakvinus.tw.	0
45. tocilizumab.tw.	1,510
46. actemra.tw.	22
47. baricitinib.tw.	19
48. LY3009104.tw.	2
49. sarilumab.tw.	17
50. SAR153191.tw.	0
51. REGN88.tw.	1
52. Randomized Controlled Trials as Topic/	109,420
53. randomized controlled trial/	428,912
54. Random Allocation/	88,469
55. Double Blind Method/	138,763
56. Single Blind Method/	22,673
57. clinical trial/	505,164
58. clinical trial, phase i.pt.	16,599
59. clinical trial, phase ii.pt.	26,972
60. clinical trial, phase iii.pt.	11,812
61. clinical trial, phase iv.pt.	1,228
62. controlled clinical trial.pt.	91,593
63. randomized controlled trial.pt.	428,912
64. multicenter study.pt.	209,949
65. clinical trial.pt.	505,164
66. exp Clinical Trials as topic/	301,158
67. 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66	1,159,034
68. (clinical adj trial$).tw.	273,192
69. ((singl$ or doubl$ or treb$ or tripl$) adj (blind$3 or mask$3)).tw.	147,350
70. placebos/	33,635
71. placebo$.tw.	184,038
72. randomly allocated.tw.	21,350
73. (allocated adj2 random$).tw.	24,207
74. 68 or 69 or 70 or 71 or 72 or 73	505,881
75. 67 or 74	1,353,869
76. case report.tw.	245,662
77. letter/	938,172
78. historical article/	335,811

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Supplemental Table 2: MEDLINE literature search strategy

Search term	Hits
79. 76 or 77 or 78	1,506,289
80. 75 not 79	1,321,930
81. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12	133,177
82. or/13-51	68,429
83. 80 and 81 and 82	3,671
84. limit 83 to (english language and yr="1990 -Current")	3,292

Supplemental Table 3: CENTRAL literature search strategy

Search term	Hits
1. MeSH descriptor: [Arthritis, Rheumatoid] explode all trees	4,480
2. MeSH descriptor: [Rheumatoid Nodule] this term only	11
3. Rheumatoid arthritis: ti,ab,kw	7,456
4. Methotrexate:ti,ab,kw	6,622
5. Mexate:ti,ab,kw	0
6. Amethopterin:ti,ab,kw	12
7. Trexall:ti,ab,kw	0
8. Rheumatrex:ti,ab,kw	0
9. Adalimumab:ti,ab,kw	968
10. Humira:ti,ab,kw	38
11. Infliximab:ti,ab,kw	1,174
12. Remicade:ti,ab,kw	38
13. Etanercept:ti,ab,kw	1,022
14. Enbrel:ti,ab,kw	43
15. Certolizumab:ti,ab,kw	209
16. Cimzia:ti,ab,kw	8
17. Golimumab:ti,ab,kw	264
18. Simponi:ti,ab,kw	6
19. Sulfasalazine: ti,ab,kw	629
20. Salazosulfapyridine:ti,ab,kw	392
21. Azulfidine:ti,ab,kw	15
22. Sulfazine:ti,ab, kw	0
23. Salazopyrin:ti,ab,kw	28
24. Hydroxychloroquine:ti,b,kw	442
25. Plaquenil:ti,ab,kw	9
26. anakinra:ti,ab,kw	94
27. kineret:ti,ab,kw	5
28. abatacept:ti,ab,kw	283
29. orencia:ti,ab,kw	4
30. rituximab:ti,ab,kw	1,571
31. mabthera:ti,ab,kw	43
32. rituxan:ti,ab,kw	23
33. tofacitinib:ti,ab,kw	127
34. xeljanz:ti,ab,kw	0
35. jakvinus:ti,ab,kw	0
36. tocilizumab:ti,ab,kw	257
37. actemra:ti,ab,kw	5
38. baricitinib:ti,ab,kw	26
39. LY3009104:ti,ab,kw	13

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Supplemental Table 3: CENTRAL literature search strategy

Search term	Hits
40. sarilumab:ti,ab,kw	20
41. SAR153191:ti,ab,kw	0
42. REGN88:ti,ab,kw	0
43. 1 OR 2 OR 3	8,119
44. #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42	10,993
45. #44 AND #43 (Publication Year from 1990 to 2016, in Trials)	2,407

Supplemental Table 4: Studies evaluating bDMARDs among bDMARD-naive cDMARD-IR RA patients

Author	Title (primary publication)
Bae 2016	A phase III, multicentre, randomised, double-blind, active-controlled, parallel-group trial comparing safety and efficacy of HD203, with innovator etanercept, in combination with methotrexate, in patients with rheumatoid arthritis: the HERA study
Burmester 2014	A randomised, double-blind, parallel-group study of the safety and efficacy of subcutaneous tocilizumab versus intravenous tocilizumab in combination with traditional disease-modifying antirheumatic drugs in patients with moderate to severe rheumatoid arthritis (SUMMACTA study)
Choe 2015	A randomised, double-blind, phase III study comparing SB2, an infliximab biosimilar, to the infliximab reference product Remicade in patients with moderate to severe rheumatoid arthritis despite methotrexate therapy
Choy 2012	Certolizumab pegol plus MTX administered every 4 weeks is effective in patients with RA who are partial responders to MTX
Combe 2006	Etanercept and sulfasalazine, alone and combined, in patients with active rheumatoid arthritis despite receiving sulfasalazine: a double-blind comparison
De Filippis 2006	Improving outcomes in tumour necrosis factor a treatment: comparison of the efficacy of the tumour necrosis factor a blocking agents etanercept and infliximab in patients with active rheumatoid arthritis.
Dougados 2013	Adding tocilizumab or switching to tocilizumab monotherapy in methotrexate inadequate responders: 24-week symptomatic and structural results of a 2-year randomised controlled strategy trial in rheumatoid arthritis (ACT-RAY)
Dougados 2015	Baricitinib, an oral janus kinase JAK1/JAK2 inhibitor, in patients with active rheumatoid arthritis (RA) and an inadequate response to cDMARD therapy: results of the phase 3 RA-build study
Emery 2006	The Efficacy and Safety of Rituximab in Patients With Active Rheumatoid Arthritis Despite Methotrexate Treatment: Results of a Phase IIb Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Trial
Emery 2010	Efficacy and safety of different doses and retreatment of rituximab: a randomised, placebo-controlled trial in patients who are biological naïve with active rheumatoid arthritis and an inadequate response to methotrexate (Study Evaluating Rituximab's Efficacy in MTX iNadequate rEsponders (SERENE))
Emery 2015	A phase III randomised, double-blind, parallel-group study comparing SB4 with etanercept reference product in patients with active rheumatoid arthritis despite methotrexate therapy
Fleischmann 2009	Efficacy and safety of certolizumab pegol monotherapy every 4 weeks in patients with rheumatoid arthritis failing previous diseasemodifying antirheumatic therapy: the FAST4WARD study
Fleischmann 2012	Placebo-Controlled Trial of Tofacitinib Monotherapy in Rheumatoid Arthritis
Fleischmann 2012-2	Phase IIb Dose-Ranging Study of the Oral JAK Inhibitor Tofacitinib (CP-690,550) or Adalimumab Monotherapy Versus Placebo in Patients With Active Rheumatoid Arthritis With an Inadequate Response to Disease-Modifying Antirheumatic Drug
Furst 2003	Adalimumab, a Fully Human Anti–Tumor Necrosis Factor-α Monoclonal Antibody, and Concomitant Standard Antirheumatic Therapy for the Treatment of Rheumatoid Arthritis: Results of STAR (Safety Trial of Adalimumab in Rheumatoid Arthritis)
Gabay 2013	Tocilizumab monotherapy versus adalimumab monotherapy for treatment of rheumatoid arthritis (ADACTA): a randomised, double-blind, controlled phase 4 trial
Genovese 2004	Combination Therapy With Etanercept and Anakinra in the Treatment of Patients With Rheumatoid Arthritis Who Have Been Treated Unsuccessfully With Methotrexate
Genovese 2008	Interleukin-6 receptor inhibition with tocilizumab reduces disease activity in rheumatoid arthritis with inadequate response to disease-modifying antirheumatic drugs: the tocilizumab in combination with traditional disease-modifying antirheumatic drug therapy study
Genovese 2011	Subcutaneous abatacept versus intravenous abatacept: A phase IIIb noninferiority study in patients with an inadequate response to methotrexate
Genovese 2015	Sarilumab Plus Methotrexate in Patients With Active Rheumatoid Arthritis and Inadequate Response to Methotrexate Results of a Phase III Study

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Supplemental Table 4: Studies evaluating bDMARDs among bDMARD-naive cDMARD-IR RA patients

Author	Title (primary publication)
Iwahashi 2014	Efficacy, safety, pharmacokinetics and immunogenicity of abatacept administered subcutaneously or intravenously in Japanese patients with rheumatoid arthritis and inadequate response to methotrexate: a Phase II/III, randomized study
Jobanpurta 2012	A randomised efficacy and discontinuation study of etanercept versus adalimumab (REDSEA) for rheumatoid arthritis: apragmatic, unblinded, non-inferiority study of first TNF inhibitoruse:outcomes over 2 years
Johnsen 2006	Comparison of 2 Doses of Etanercept (50 vs 100 mg) in Active Rheumatoid Arthritis: ARandomized Double Blind Study
Kameda 2010	Etanercept (ETN) with methotrexate (MTX) is better than ETN monotherapy in patients with active rheumatoid arthritis despite MTX therapy: a randomized trial
Kay 2008	Golimumab in Patients With Active Rheumatoid Arthritis Despite Treatment With Methotrexate
Keystone 2004	Radiographic, Clinical, and Functional Outcomes of Treatment With Adalimumab (a Human Anti–Tumor Necrosis Factor Monoclonal Antibody) in Patients With Active Rheumatoid Arthritis Receiving Concomitant Methotrexate Therapy
Keystone 2008	Certolizumab Pegol Plus Methotrexate Is Significantly More Effective Than Placebo Plus Methotrexate in Active Rheumatoid Arthritis (RAPID 1)
Keystone 2009	Golimumab, a human antibody to tumour necrosis factor a given by monthly subcutaneous injections, in active rheumatoid arthritis despite methotrexate therapy: the GO-FORWARD Study
Keystone 2012	Clinical evaluation of the efficacy of the P2X 7 purinergic receptor antagonist AZD9056 on the signs and symptoms of rheumatoid arthritis in patients with active disease despite treatment with methotrexate or sulphasalazine
Keystone 2015	Safety and efficacy of baricitinib at 24 weeks in patients with rheumatoid arthritis who have had an inadequate response to methotrexate
Kim 2007	A randomized, double-blind, placebo-controlled, phase III study of the human anti-tumor necrosis factor antibody adalimumab administered as subcutaneous injections in Korean rheumatoid arthritis patients treated with methotrexate
Kim 2013	A Clinical Trial and Extension Study of Infliximab in Korean Patients with Active Rheumatoid Arthritis despite Methotrexate Treatment
Klareskog 2004	Therapeutic effect of the combination of etanercept and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomised controlled trial
Kremer 2003	Treatment of Rheumatoid Arthritis by Selective Inhibition of T-Cell Activation with Fusion Protein CTLA4Ig
Kremer 2006	Effects of Abatacept in Patients with Methotrexate-Resistant Active Rheumatoid Arthritis
Kremer 2011	Tocilizumab inhibits structural joint damage in rheumatoid arthritis patients with inadequate responses to methotrexate: results from the double-blind treatment phase of a randomized placebo-controlled trial of tocilizumab safety and prevention of structural joint damage at one year
Kremer 2012	A Phase IIb Dose-Ranging Study of the Oral JAK Inhibitor Tofacitinib (CP-690,550) Versus Placebo in Combination With Background Methotrexate in Patients With Active Rheumatoid Arthritis and an Inadequate Response to Methotrexate Alone
Kremer 2013	Tofacitinib in combination with nonbiologic disease-modifying antirheumatic drugs in patients with active rheumatoid arthritis: a randomized trial
Li 2015	Efficacy and safety results from a Phase 3, randomized, placebo-controlled trial of subcutaneous golimumab in Chinese patients with active rheumatoid arthritis despite methotrexate therapy
Machado 2014	Open-Label Observation of Addition of Etanercept Versus a Conventional Disease-Modifying Antirheumatic Drug in Subjects With Active Rheumatoid Arthritis Despite Methotrexate Therapy in the Latin American Region
Maini 1998	Therapeutic efficacy of multiple intravenous infusions of anti-tumor necrosis factor ci! monoclonal antibody combined with low-dose weekly methotrexate in rheumatoid arthritis

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Supplemental Table 4: Studies evaluating bDMARDs among bDMARD-naive cDMARD-IR RA patients

Author	Title (primary publication)
Maini 1999	Infliximab (chimeric anti-tumour necrosis factor monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomised phase III trial
Miyasaka 2008	Clinical investigation in highly disease-affected rheumatoid arthritis patients in Japan with adalimumab applying standard and general evaluation: the CHANGE study
Moreland 1999	Etanercept Therapy in Rheumatoid Arthritis, A Randomized, Controlled Trial
Nishimoto 2007	Study of active controlled monotherapy used for rheumatoid arthritis, an IL-6 inhibitor (SAMURAI): evidence of clinical and radiographic benefit from an x ray reader-blinded randomised controlled trial of tocilizumab
Nishimoto 2009	Study of active controlled tocilizumab monotherapy for rheumatoid arthritis patients with an inadequate response to methotrexate (SATORI): significant reduction in disease activity and serum vascular endothelial growth factor by IL-6 receptor inhibition therapy
O'Dell 2002	Treatment of rheumatoid arthritis with methotrexate and hydroxychloroquine, methotrexate and sulfasalazine, or a combination of the three medications: Results of a Two-Year, Randomized, Double-Blind, Placebo-Controlled Trial
O'Dell 2013	Therapies for Active Rheumatoid Arthritis after Methotrexate Failure
Ogata 2014	Phase III study of the efficacy and safety of subcutaneous versus intravenous tocilizumab monotherapy in patients with rheumatoid arthritis
Peterfy 2016	MRI assessment of suppression of structural damage in patients with rheumatoid arthritis receiving rituximab: results from the randomised, placebo-controlled, double-blind RA-SCORE study
Pope 2014	The Canadian Methotrexate and Etanercept Outcome Study: a randomised trial of discontinuing versus continuing methotrexate after 6 months of etanercept and methotrexate therapy in rheumatoid arthritis
Rubbert 2010	Efficacy and safety of various repeat treatment dosing regimens of rituximab in patients with active rheumatoid arthritis: results of a Phase III randomized study (MIRROR)
Schiff 2008	Efficacy and safety of abatacept or infliximab vs placebo in ATTEST: a phase III, multi-centre, randomised, double-blind, placebo-controlled study in patients with rheumatoid arthritis and an inadequate response to methotrexate
Smolen 2008	Effect of interleukin-6 receptor inhibition with tocilizumab in patients with rheumatoid arthritis (OPTION study): a double-blind, placebo-controlled, randomised trial
Smolen 2009	Efficacy and safety of certolizumab pegol plus methotrexate in active rheumatoid arthritis: the RAPID 2 study. A randomised controlled trial
Smolen 2015	Certolizumab pegol in rheumatoid arthritis patients with low to moderate activity: the CERTAIN double-blind, randomised, placebo-controlled trial
Takeuchi 2009	Impact of trough serum level on radiographic and clinical response to infliximab plus methotrexate in patients with rheumatoid arthritis: results from the RISING study
Takeuchi 2013	Phase II dose–response study of abatacept in Japanese patients with active rheumatoid arthritis with an inadequate response to methotrexate
Takeuchi 2013-3	A phase 3 randomized, double-blind, multicenter comparative study evaluating the effect of etanercept versus methotrexate on radiographic outcomes, disease activity, and safety in Japanese subjects with active rheumatoid arthritis
Takeuchi 2015	Evaluation of the pharmacokinetic equivalence and 54-week efficacy and safety of CT-P13 and innovator infliximab in Japanese patients with rheumatoid arthritis
Tam 2012	Infliximab is Associated with Improvement in Arterial Stiffness in Patients with Early Rheumatoid Arthritis —A Randomized Trial
Tanaka 2012	A Study on the Selection of DMARDs for the Combination Therapy with Adalimumab
Tanaka 2012-2	Golimumab in combination with methotrexate in Japanese patients with active rheumatoid arthritis: results of the GO-FORTH study

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Supplemental Table 4: Studies evaluating bDMARDs among bDMARD-naive cDMARD-IR RA patients

Author	Title (primary publication)
Taylor 2004	Comparison of Ultrasonographic Assessment of Synovitis and Joint Vascularity With Radiographic Evaluation in a Randomized, Placebo-Controlled Study of Infliximab Therapy in Early Rheumatoid Arthritis
Van de heijde 2013	Tofacitinib (CP-690,550) in Patients With Rheumatoid Arthritis Receiving Methotrexate: Twelve-Month Data From a Twenty-Four–Month Phase III Randomized Radiographic Study
van de Putte 2004	Efficacy and safety of adalimumab as monotherapy in patients with rheumatoid arthritis for whom previous disease modifying antirheumatic drug treatment has failed
van Vollenhoven 2009	Addition of infliximab compared with addition of sulfasalazine and hydroxychloroquine to methotrexate in patients with early rheumatoid arthritis (Swefot trial): 1-year results of a randomised trial
van Vollenhoven 2011	Atacicept in Patients With Rheumatoid Arthritis and an Inadequate Response to Methotrexate, Results of a Phase II, Randomized, Placebo-Controlled Trial
van Vollenhoven 2012	Tofacitinib or Adalimumab versus Placebo in Rheumatoid Arthritis
Vital 2015	An extra dose of rituximab improves clinical response in rheumatoid arthritis patients with initial incomplete B cell depletion: a randomised controlled trial
Wada 2012	Clinical and radiographic results from a 2-year comparison of once-weekly versus twice-weekly administration of etanercept in biologics-naive patients with rheumatoid arthritis
Weinblatt 1999	A trial of etanercept, a recombinant tumor necrosis factor receptor: fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate
Weinblatt 2003	Adalimumab, a Fully Human Anti–Tumor Necrosis Factor Monoclonal Antibody, for the Treatment of Rheumatoid Arthritis in Patients Taking Concomitant Methotrexate (The ARMADA Trial)
Weinblatt 2013	Head-to-Head Comparison of Subcutaneous Abatacept Versus Adalimumab for Rheumatoid Arthritis
Westhovens 2006	The Safety of Infliximab, Combined With Background Treatments, Among Patients With Rheumatoid Arthritis and Various Comorbidities
Yamamoto 2014	Efficacy and safety of certolizumab pegol plus methotrexate in Japanese rheumatoid arthritis patients with an inadequate response to methotrexate: the J-RAPID randomized, placebo-controlled trial
Yamamoto 2014-2	Efficacy and safety of certolizumab pegol without methotrexate co-administration in Japanese patients with active rheumatoid arthritis: The HIKARI randomized, placebo-controlled trial
Yazici 2012	Efficacy of tocilizumab in patients with moderate to severe active rheumatoid arthritis and a previous inadequate response to disease-modifying antirheumatic drugs: the ROSE study
Yoo 2013	A randomized, double-blind, parallel group study to demonstrate equivalence in efficacy and safety of CT-P13 compares with innovator infliximab when coadminstered with methotrexate in patients with active rheumatoid arthritis

Supplemental Table 5: Conditional probability of EULAR response given ACR response

	Eular response		
ACR response	No response	Moderate response	Good response
ACR < 20	0.796	0.143	0.060
ACR 20-50	0.070	0.474	0.456
ACR 50-70	0.143	0.143	0.714
ACR 70+	0.000	0.500	0.500

Supplemental Table 6: Posterior distribution of input parameters in PSA

Group	Parameter	Mean	SD	2.5%	97.5%	Distribution	Source
Log odds mortality	Baseline HAQ	0.80	0.11	0.60	1.03	Normal	Wolfe2003
Log hazard ratio mortality	Change in HAQ from baseline months 0 - 6	0.11	0.02	0.08	0.15	Normal	Michaud2012
Log hazard ratio mortality	Change in HAQ from baseline months >6 - 12	0.15	0.02	0.10	0.19	Normal	Michaud2012
Log hazard ratio mortality	Change in HAQ from baseline months >12 - 24	0.15	0.02	0.10	0.19	Normal	Michaud2012
Log hazard ratio mortality	Change in HAQ from baseline months >24 - 36	0.19	0.03	0.13	0.25	Normal	Michaud2012
Log hazard ratio mortality	Change in HAQ from baseline months >36	0.17	0.03	0.11	0.24	Normal	Michaud2012
Treatment duration - moderate	Mean (log)	3.00	0.01	2.97	3.03	Multivariate normal	Stevenson2016
Treatment duration - moderate	SE (log)	0.39	0.01	0.38	0.41	Multivariate normal	Stevenson2016
Treatment duration - good	Mean (log)	3.70	0.01	3.67	3.73	Multivariate normal	Stevenson2016
Treatment duration - good	SE (log)	0.42	0.01	0.40	0.43	Multivariate normal	Stevenson2016
NMA ACR response (probit scale) 1st line	cDMARDs mean	0.54	0.00	0.54	0.54	Normal	NMA
NMA ACR response (probit scale) 1st line	Cutpoint ACR50	0.62	0.01	0.61	0.63	Normal	NMA
NMA ACR response (probit scale) 1st line	Cutpoint ACR70	1.21	0.01	1.19	1.23	Normal	NMA
NMA ACR response (probit scale) 1st line	cDMARDs	0.00	0.00	0.00	0.00	Normal	NMA
NMA ACR response (probit scale) 1st line	ABT IV + MTX	-0.81	0.12	-1.03	-0.58	Normal	NMA
NMA ACR response (probit scale) 1st line	ADA + MTX	-0.77	0.11	-0.98	-0.56	Normal	NMA
NMA ACR response (probit scale) 1st line	ADA	-0.35	0.22	-0.79	0.07	Normal	NMA
NMA ACR response (probit scale) 1st line	Triple therapy	-0.74	0.29	-1.29	-0.20	Normal	NMA
NMA ACR response (probit scale) 1st line	ETN + MTX	-0.87	0.11	-1.06	-0.64	Normal	NMA
NMA ACR response (probit scale) 1st line	ETN	-0.54	0.15	-0.82	-0.26	Normal	NMA
NMA ACR response (probit scale) 1st line	GOL + MTX	-0.82	0.15	-1.11	-0.51	Normal	NMA
NMA ACR response (probit scale) 1st line	IFX + MTX	-0.77	0.14	-1.05	-0.48	Normal	NMA

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Supplemental Table 6: Posterior distribution of input parameters in PSA

Group	Parameter	Mean	SD	2.5%	97.5%	Distribution	Source
NMA ACR response (probit scale) 1st line	Placebo					Normal	NMA
NMA ACR response (probit scale) 1st line	TCZ + MTX	-0.79	0.26	-1.26	-0.29	Normal	NMA
NMA ACR response (probit scale) 1st line	TCZ	-0.86	0.32	-1.50	-0.24	Normal	NMA
NMA ACR response (probit scale) 1st line	CZP + MTX	-1.20	0.12	-1.46	-0.97	Normal	NMA
NMA ACR response (probit scale) 1st line	ABT SC + MTX	-0.81	0.11	-1.03	-0.58	Normal	NMA
NMA ACR response (probit scale) 1st line	NBT					Normal	NMA
NMA ACR response (probit scale) 1st line	RTX + MTX	-0.67	0.15	-0.97	-0.36	Normal	NMA
NMA ACR response (probit scale) 1st line	TOF + MTX	-0.75	0.14	-1.04	-0.49	Normal	NMA
NMA ACR response (probit scale) 1st line	RTX	-0.57	0.21	-0.96	-0.20	Normal	NMA
NMA ACR response (probit scale) 1st line	TOF	-0.16	0.41	-0.93	0.67	Normal	NMA
NMA ACR response (probit scale) 1st line	CZP	-0.52	0.40	-1.31	0.28	Normal	NMA
NMA ACR response (probit scale) 1st line	GOL	0.23	0.34	-0.49	0.92	Normal	NMA
ACR response (probit scale) 2+ lines	cDMARDs mean	0.79	0.05	0.70	0.89	Normal	Smolen2015
ACR response (probit scale) 2+ lines	Cutpoint ACR50	0.63	0.05	0.53	0.73	Normal	Smolen2015
ACR response (probit scale) 2+ lines	Cutpoint ACR70	1.30	0.05	1.20	1.40	Normal	Smolen2015
ACR response (probit scale) 2+ lines	cDMARDs	0.00	0.00	0.00	0.00	Normal	Smolen2015
ACR response (probit scale) 2+ lines	ABT IV + MTX	-0.81	0.13	-1.09	-0.55	Normal	Smolen2015
ACR response (probit scale) 2+ lines	ADA + MTX	-0.77	0.11	-0.98	-0.55	Normal	Smolen2015
ACR response (probit scale) 2+ lines	ADA	-0.35	0.22	-0.77	0.03	Normal	Smolen2015
ACR response (probit scale) 2+ lines	Triple therapy	-0.69	0.28	-1.25	-0.13	Normal	Smolen2015
ACR response (probit scale) 2+ lines	ETN + MTX	-0.89	0.12	-1.15	-0.64	Normal	Smolen2015
ACR response (probit scale) 2+ lines	ETN	-0.55	0.16	-0.84	-0.24	Normal	Smolen2015
ACR response (probit scale) 2+ lines	GOL + MTX	-0.81	0.15	-1.09	-0.52	Normal	Smolen2015
ACR response (probit scale) 2+ lines	IFX + MTX	-0.77	0.15	-1.04	-0.51	Normal	Smolen2015

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Supplemental Table 6: Posterior distribution of input parameters in PSA

Group	Parameter	Mean	SD	2.5%	97.5%	Distribution	Source
ACR response (probit scale) 2+ lines	Placebo					Normal	Smolen2015
ACR response (probit scale) 2+ lines	TCZ + MTX	-0.80	0.27	-1.26	-0.24	Normal	Smolen2015
ACR response (probit scale) 2+ lines	TCZ	-0.85	0.31	-1.46	-0.20	Normal	Smolen2015
ACR response (probit scale) 2+ lines	CZP + MTX	-1.19	0.12	-1.42	-0.96	Normal	Smolen2015
ACR response (probit scale) 2+ lines	ABT SC + MTX	-0.82	0.13	-1.09	-0.56	Normal	Smolen2015
ACR response (probit scale) 2+ lines	NBT					Normal	Smolen2015
ACR response (probit scale) 2+ lines	RTX + MTX	-0.69	0.18	-1.02	-0.37	Normal	Smolen2015
ACR response (probit scale) 2+ lines	TOF + MTX	-0.74	0.15	-1.05	-0.48	Normal	Smolen2015
ACR response (probit scale) 2+ lines	RTX	-0.60	0.21	-0.99	-0.18	Normal	Smolen2015
ACR response (probit scale) 2+ lines	TOF	-0.12	0.39	-0.82	0.63	Normal	Smolen2015
ACR response (probit scale) 2+ lines	CZP	-0.42	0.38	-1.21	0.35	Normal	Smolen2015
ACR response (probit scale) 2+ lines	GOL	0.22	0.35	-0.49	0.84	Normal	Smolen2015
HAQ change by Eular response	No response	0.00	0.00	0.00	0.00	Normal	Stevenson2016
HAQ change by Eular response	Moderate response	-0.32	0.05	-0.40	-0.22	Normal	Stevenson2016
HAQ change by Eular response	Good response	-0.67	0.11	-0.85	-0.45	Normal	Stevenson2016
Yearly HAQ progression by therapy	cDMARDs	0.03	0.00	0.03	0.04	Normal	Wolfe2010
Yearly HAQ progression by therapy	ABT IV + MTX	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	ADA + MTX	-0.00	0.01	-0.02	0.01	Normal	Wolfe2010
Yearly HAQ progression by therapy	ADA	0.01	0.01	0.00	0.03	Normal	Wolfe2010
Yearly HAQ progression by therapy	Triple therapy	0.03	0.00	0.03	0.04	Normal	Wolfe2010
Yearly HAQ progression by therapy	ETN + MTX	-0.01	0.00	-0.01	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	ETN	-0.00	0.00	-0.01	0.01	Normal	Wolfe2010
Yearly HAQ progression by therapy	GOL + MTX	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	IFX + MTX	-0.00	0.00	-0.01	0.01	Normal	Wolfe2010

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Supplemental Table 6: Posterior distribution of input parameters in PSA

Group	Parameter	Mean	SD	2.5%	97.5%	Distribution	Source
Yearly HAQ progression by therapy	Placebo	0.03	0.00	0.03	0.04	Normal	Wolfe2010
Yearly HAQ progression by therapy	TCZ + MTX	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	TCZ	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	CZP + MTX	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	ABT SC + MTX	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	NBT	0.03	0.00	0.03	0.04	Normal	Wolfe2010
Yearly HAQ progression by therapy	RTX + MTX	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	TOF + MTX	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	RTX	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	TOF	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	CZP	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by therapy	GOL	-0.00	0.00	-0.00	0.00	Normal	Wolfe2010
Yearly HAQ progression by age relative to overall	< 40	-0.02	0.00	-0.02	-0.02	Normal	Michaud2011
Yearly HAQ progression by age relative to overall	40-64	-0.01	0.00	-0.01	-0.01	Normal	Michaud2011
Yearly HAQ progression by age relative to overall	>= 65	0.02	0.00	0.01	0.02	Normal	Michaud2011
Treatment cost	Cost first 6 months - cDMARDs	590.02	0.00	590.02	590.02	Fixed	Label
Treatment cost	Cost first 6 months - ABT IV + MTX	17545.51	0.00	17545.51	17545.51	Fixed	Label
Treatment cost	Cost first 6 months - ADA + MTX	20797.66	0.00	20797.66	20797.66	Fixed	Label
Treatment cost	Cost first 6 months - ADA	20207.64	0.00	20207.64	20207.64	Fixed	Label
Treatment cost	Cost first 6 months - Triple therapy	1612.25	0.00	1612.25	1612.25	Fixed	Label
Treatment cost	Cost first 6 months - ETN + MTX	20801.12	0.00	20801.12	20801.12	Fixed	Label
Treatment cost	Cost first 6 months - ETN	20211.10	0.00	20211.10	20211.10	Fixed	Label
Treatment cost	Cost first 6 months - GOL + MTX	16596.98	0.00	16596.98	16596.98	Fixed	Label
Treatment cost	Cost first 6 months - IFX + MTX	13099.36	0.00	13099.36	13099.36	Fixed	Label

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Supplemental Table 6: Posterior distribution of input parameters in PSA

Group	Parameter	Mean	SD	2.5%	97.5%	Distribution	Source
Treatment cost	Cost first 6 months - Placebo	0.00	0.00	0.00	0.00	Fixed	Label
Treatment cost	Cost first 6 months - TCZ + MTX	8764.64	0.00	8764.64	8764.64	Fixed	Label
Treatment cost	Cost first 6 months - TCZ	8174.62	0.00	8174.62	8174.62	Fixed	Label
Treatment cost	Cost first 6 months - CZP + MTX	21197.29	0.00	21197.29	21197.29	Fixed	Label
Treatment cost	Cost first 6 months - ABT SC + MTX	20129.41	0.00	20129.41	20129.41	Fixed	Label
Treatment cost	Cost first 6 months - NBT	590.02	0.00	590.02	590.02	Fixed	Label
Treatment cost	Cost first 6 months - RTX + MTX	24632.18	0.00	24632.18	24632.18	Fixed	Label
Treatment cost	Cost first 6 months - TOF + MTX	16708.67	0.00	16708.67	16708.67	Fixed	Label
Treatment cost	Cost first 6 months - RTX	24042.16	0.00	24042.16	24042.16	Fixed	Label
Treatment cost	Cost first 6 months - TOF	16118.65	0.00	16118.65	16118.65	Fixed	Label
Treatment cost	Cost first 6 months - CZP	20607.27	0.00	20607.27	20607.27	Fixed	Label
Treatment cost	Cost first 6 months - GOL	16006.96	0.00	16006.96	16006.96	Fixed	Label
Treatment cost	Annual cost 6+ months - cDMARDs	1180.04	0.00	1180.04	1180.04	Fixed	Label
Treatment cost	Annual cost 6+ months - ABT IV + MTX	28732.71	0.00	28732.71	28732.71	Fixed	Label
Treatment cost	Annual cost 6+ months - ADA + MTX	41595.33	0.00	41595.33	41595.33	Fixed	Label
Treatment cost	Annual cost 6+ months - ADA	40415.28	0.00	40415.28	40415.28	Fixed	Label
Treatment cost	Annual cost 6+ months - Triple therapy	3279.59	0.00	3279.59	3279.59	Fixed	Label
Treatment cost	Annual cost 6+ months - ETN + MTX	41602.24	0.00	41602.24	41602.24	Fixed	Label
Treatment cost	Annual cost 6+ months - ETN	40422.20	0.00	40422.20	40422.20	Fixed	Label
Treatment cost	Annual cost 6+ months - GOL + MTX	33193.95	0.00	33193.95	33193.95	Fixed	Label
Treatment cost	Annual cost 6+ months - IFX + MTX	37814.54	0.00	37814.54	37814.54	Fixed	Label

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Supplemental Table 6: Posterior distribution of input parameters in PSA

Group	Parameter	Mean	SD	2.5%	97.5%	Distribution	Source
Treatment cost	Annual cost 6+ months - Placebo	0.00	0.00	0.00	0.00	Fixed	Label
Treatment cost	Annual cost 6+ months - TCZ + MTX	17529.28	0.00	17529.28	17529.28	Fixed	Label
Treatment cost	Annual cost 6+ months - TCZ	16349.24	0.00	16349.24	16349.24	Fixed	Label
Treatment cost	Annual cost 6+ months - CZP + MTX	34666.86	0.00	34666.86	34666.86	Fixed	Label
Treatment cost	Annual cost 6+ months - ABT SC + MTX	36019.94	0.00	36019.94	36019.94	Fixed	Label
Treatment cost	Annual cost 6+ months - NBT	1180.04	0.00	1180.04	1180.04	Fixed	Label
Treatment cost	Annual cost 6+ months - RTX + MTX	27225.72	0.00	27225.72	27225.72	Fixed	Label
Treatment cost	Annual cost 6+ months - TOF + MTX	33417.34	0.00	33417.34	33417.34	Fixed	Label
Treatment cost	Annual cost 6+ months - RTX	26045.67	0.00	26045.67	26045.67	Fixed	Label
Treatment cost	Annual cost 6+ months - TOF	32237.30	0.00	32237.30	32237.30	Fixed	Label
Treatment cost	Annual cost 6+ months - CZP	33486.82	0.00	33486.82	33486.82	Fixed	Label
Treatment cost	Annual cost 6+ months - GOL	32013.91	0.00	32013.91	32013.91	Fixed	Label
Days in hospital per year	HAQ: 0 - <0.5	0.26	0.52	0.00	1.52	Gamma	Carlson2015
Days in hospital per year	HAQ: 0.5 - <1	0.09	0.34	0.00	0.94	Gamma	Carlson2015
Days in hospital per year	HAQ: 1 - <1.5	0.47	0.45	0.02	1.75	Gamma	Carlson2015
Days in hospital per year	HAQ: 1.5 - <2	0.65	0.41	0.12	1.79	Gamma	Carlson2015
Days in hospital per year	HAQ: 2 - <2.5	1.86	0.48	1.04	2.84	Gamma	Carlson2015
Days in hospital per year	HAQ: >2.5	4.22	0.50	3.39	5.35	Gamma	Carlson2015
Cost per day in hospital	HAQ: 0 - <0.5	1244.94	186.63	890.06	1635.96	Gamma	Carlson2015
Cost per day in hospital	HAQ: 0.5 - <1	1248.82	188.63	909.64	1592.29	Gamma	Carlson2015
Cost per day in hospital	HAQ: 1 - <1.5	1265.82	202.35	914.06	1662.36	Gamma	Carlson2015
Cost per day in hospital	HAQ: 1.5 - <2	1259.83	195.59	942.09	1664.06	Gamma	Carlson2015
Cost per day in hospital	HAQ: 2 - <2.5	1234.18	200.57	871.11	1668.98	Gamma	Carlson2015
Cost per day in hospital	HAQ: >2.5	1242.80	174.76	928.76	1602.31	Gamma	Carlson2015

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Supplemental Table 6: Posterior distribution of input parameters in PSA

Group	Parameter	Mean	SD	2.5%	97.5%	Distribution	Source
General management cost	Chest x-ray	108.99	6.02	98.28	121.15	Gamma	Claxton2016
General management cost	X-ray visit	53.55	3.94	45.96	61.70	Gamma	Claxton2016
General management cost	Outpatient followup	188.04	13.80	162.04	214.15	Gamma	Claxton2016
General management cost	Mantoux tuberculin skin test	30.50	0.00	30.50	30.50	Fixed	Claxton2016
Productivity loss	Regression coefficient - HAQ	5812.32	1462.19	2905.60	8801.85	Normal	Wolfe2005
Serious infection rate	cDMARDs	0.03	0.00	0.03	0.03	Lognormal	Stevenson2016
Serious infection rate	ABT IV + MTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	ADA + MTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	ADA	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	Triple therapy	0.03	0.00	0.03	0.03	Lognormal	Stevenson2016
Serious infection rate	ETN + MTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	ETN	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	GOL + MTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	IFX + MTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	Placebo	0.00	0.00	0.00	0.00	Lognormal	Stevenson2016
Serious infection rate	TCZ + MTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	TCZ	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	CZP + MTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	ABT SC + MTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	NBT	0.00	0.00	0.00	0.00	Lognormal	Stevenson2016
Serious infection rate	RTX + MTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	TOF + MTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	RTX	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	TOF	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	CZP	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection rate	GOL	0.04	0.00	0.04	0.04	Lognormal	Stevenson2016
Serious infection cost	Cost per pneumonia hospitalization	5826.20	654.89	4812.54	6984.86	Normal	CMS2016
Serious infection utility loss	One month loss in utility	0.16	0.00	0.16	0.16	Fixed	Stevenson2016
Utility	Class 1 predictors - Intercept	0.81	0.00	0.81	0.82	Multivariate normal	Hernandez2013
Utility	Class 1 predictors - HAQ	-0.09	0.00	-0.10	-0.09	Multivariate normal	Hernandez2013
Utility	Class 1 predictors - HAQ^2	0.00	0.00	-0.00	0.00	Multivariate normal	Hernandez2013
Utility	Class 1 predictors - Pain/100	-0.06	0.00	-0.06	-0.05	Multivariate normal	Hernandez2013

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Supplemental Table 6: Posterior distribution of input parameters in PSA

Group	Parameter	Mean	SD	2.5%	97.5%	Distribution	Source
Utility	Class 1 predictors - Age/10k	0.00	0.00	0.00	0.01	Multivariate normal	Hernandez2013
Utility	Class 1 predictors - Age/10k^2	0.00	0.00	-0.00	0.00	Multivariate normal	Hernandez2013
Utility	Class 2 predictors - Intercept	0.43	0.02	0.39	0.45	Multivariate normal	Hernandez2013
Utility	Class 2 predictors - HAQ	0.05	0.03	-0.01	0.12	Multivariate normal	Hernandez2013
Utility	Class 2 predictors - HAQ^2	-0.05	0.01	-0.07	-0.03	Multivariate normal	Hernandez2013
Utility	Class 2 predictors - Pain/100	-0.38	0.02	-0.43	-0.34	Multivariate normal	Hernandez2013
Utility	Class 2 predictors - Age/10k	0.03	0.00	0.02	0.04	Multivariate normal	Hernandez2013
Utility	Class 2 predictors - Age/10k^2	0.00	0.00	-0.00	0.01	Multivariate normal	Hernandez2013
Utility	Class 3 predictors - Intercept	0.33	0.01	0.31	0.34	Multivariate normal	Hernandez2013
Utility	Class 3 predictors - HAQ	-0.14	0.01	-0.16	-0.13	Multivariate normal	Hernandez2013
Utility	Class 3 predictors - HAQ^2	0.02	0.00	0.01	0.02	Multivariate normal	Hernandez2013
Utility	Class 3 predictors - Pain/100	-0.08	0.01	-0.10	-0.07	Multivariate normal	Hernandez2013
Utility	Class 3 predictors - Age/10k	0.00	0.00	0.00	0.01	Multivariate normal	Hernandez2013
Utility	Class 3 predictors - Age/10k^2	0.00	0.00	-0.00	0.00	Multivariate normal	Hernandez2013
Utility	Class 4 predictors - Intercept	1.02	0.03	0.96	1.09	Multivariate normal	Hernandez2013
Utility	Class 4 predictors - HAQ	-0.19	0.08	-0.36	-0.05	Multivariate normal	Hernandez2013
Utility	Class 4 predictors - HAQ^2	0.03	0.02	-0.01	0.08	Multivariate normal	Hernandez2013
Utility	Class 4 predictors - Pain/100	-0.01	0.07	-0.14	0.10	Multivariate normal	Hernandez2013
Utility	Class 4 predictors - Age/10k	-0.00	0.01	-0.02	0.01	Multivariate normal	Hernandez2013
Utility	Class 4 predictors - Age/10k^2	0.00	0.00	-0.00	0.00	Multivariate normal	Hernandez2013
Utility	Predictor - Male	-0.03	0.00	-0.03	-0.02	Multivariate normal	Hernandez2013
Utility	Variance class 1	0.05	0.00	0.05	0.05	Multivariate normal	Hernandez2013
Utility	Variance class 2	0.15	0.01	0.14	0.16	Multivariate normal	Hernandez2013
Utility	Variance class 3	0.05	0.00	0.04	0.05	Multivariate normal	Hernandez2013

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Supplemental Table 6: Posterior distribution of input parameters in PSA

Group	Parameter	Mean	SD	2.5%	97.5%	Distribution	Source
Utility	Variance class 4	0.06	0.03	0.00	0.11	Multivariate normal	Hernandez2013
Utility	Variance	0.05	0.00	0.05	0.05	Multivariate normal	Hernandez2013
Utility	Probability of class 1 membership - Intercept	-1.28	0.07	-1.41	-1.15	Multivariate normal	Hernandez2013
Utility	Probability of class 1 membership - Haq	0.26	0.43	-0.65	1.01	Multivariate normal	Hernandez2013
Utility	Probability of class 1 membership - Pain/100	23.47	0.62	22.26	24.60	Multivariate normal	Hernandez2013
Utility	Probability of class 1 membership - $Pain/100^2$	-21.53	0.71	-22.81	-20.01	Multivariate normal	Hernandez2013
Utility	Probability of class 2 membership - Intercept	-6.66	0.27	-7.13	-6.12	Multivariate normal	Hernandez2013
Utility	Probability of class 2 membership - Haq	2.22	0.42	1.40	2.93	Multivariate normal	Hernandez2013
Utility	Probability of class 2 membership - Pain/100	18.44	1.18	16.04	20.58	Multivariate normal	Hernandez2013
Utility	Probability of class 2 membership - $Pain/100^2$	-13.82	0.79	-15.36	-12.28	Multivariate normal	Hernandez2013
Utility	Probability of class 3 membership - Intercept	-7.50	0.29	-8.06	-6.92	Multivariate normal	Hernandez2013
Utility	Probability of class 3 membership - Haq	1.07	0.43	0.18	1.80	Multivariate normal	Hernandez2013
Utility	Probability of class 3 membership - Pain/100	25.44	1.12	23.19	27.71	Multivariate normal	Hernandez2013
Utility	Probability of class 3 membership - $Pain/100^2$	-17.02	0.76	-18.64	-15.50	Multivariate normal	Hernandez2013

Supplemental Table 7: Results of model analysis - alternative scenarios

	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Sequence 1				
Incremental QALYs	2.666 (2.126 ; 3.227)	2.470 (1.989 ; 2.948)	2.470 (2.017 ; 2.932)	2.325 (1.907 ; 2.726)
Incremental costs	358,352 (322,994 ; 392,865)	351,047 (321,923 ; 378,720)	277,879 (243,460 ; 309,292)	360,081 (335,800 ; 383,215)
ICER	134,396	142,133	112,519	154,856
Sequence 2				
Incremental QALYs	2.656 (2.131 ; 3.261)	2.465 (2.048 ; 2.902)	2.466 (2.049 ; 2.898)	2.317 (1.892 ; 2.734)
Incremental costs	358,174 (327,303 ; 388,748)	353,912 (328,211 ; 379,846)	278,701 (245,150 ; 311,313)	359,871 (334,753 ; 384,214)
ICER	134,836	143,592	113,016	155,285
Sequence 3				
Incremental QALYs	2.647 (2.154 ; 3.189)	2.453 (2.022 ; 2.863)	2.467 (2.044 ; 2.932)	2.308 (1.870 ; 2.708)
Incremental costs	352,013 (320,894 ; 386,383)	343,080 (315,671 ; 370,962)	272,768 (239,740 ; 302,541)	353,677 (327,726 ; 379,403)
ICER	132,967	139,875	110,561	153,233
Sequence 4				
Incremental QALYs	2.641 (2.103 ; 3.217)	2.446 (1.989 ; 2.941)	2.467 (2.017 ; 2.920)	2.309 (1.882 ; 2.747)
Incremental costs	351,931 (318,217 ; 388,484)	344,210 (317,671 ; 373,938)	273,331 (240,793 ; 301,831)	353,549 (326,971 ; 380,103)
ICER	133,242	140,717	110,789	153,125
Sequence 5				
Incremental QALYs	2.715 (2.196 ; 3.245)	2.523 (2.052 ; 2.946)	2.535 (2.084 ; 3.012)	2.377 (1.966 ; 2.797)
Incremental costs	352,543 (318,776 ; 384,484)	339,475 (312,171 ; 367,443)	271,513 (239,474 ; 300,701)	354,550 (329,526 ; 378,828)
ICER	129,828	134,536	107,094	149,132
Sequence 6				
Incremental QALYs	2.679 (2.167 ; 3.313)	2.490 (1.994 ; 2.975)	2.493 (2.054 ; 2.968)	2.337 (1.947 ; 2.728)
Incremental costs	349,873 (318,962 ; 380,559)	345,759 (317,856 ; 372,327)	270,147 (238,434 ; 300,176)	351,741 (326,943 ; 373,984)
ICER	130,581	138,870	108,373	150,504
Sequence 7				
Incremental QALYs	2.699 (2.178 ; 3.262)	2.510 (2.043 ; 2.951)	2.523 (2.106 ; 3.018)	2.367 (1.955 ; 2.798)
Incremental costs	339,844 (310,920 ; 373,071)	327,122 (298,853 ; 354,779)	260,143 (228,877 ; 291,865)	342,260 (317,201 ; 365,658)
ICER	125,930	130,343	103,112	144,569
Sequence 8				
Incremental QALYs	2.674 (2.161 ; 3.252)	2.478 (2.039 ; 2.931)	2.487 (2.057 ; 2.931)	2.339 (1.937 ; 2.773)
Incremental costs	337,655 (306,075 ; 370,384)	330,392 (299,656 ; 358,246)	258,216 (226,721 ; 286,892)	339,909 (315,537 ; 362,796)
ICER	126,280	133,319	103,811	145,321
Sequence 9				
Incremental QALYs	2.659 (2.148 ; 3.221)	2.475 (2.006 ; 2.877)	2.487 (2.067 ; 2.972)	2.333 (1.942 ; 2.764)
Incremental costs	323,806 (292,623 ; 352,839)	311,259 (283,366 ; 337,540)	244,868 (215,136 ; 275,478)	326,018 (301,836 ; 350,474)
ICER	121,792	125,736	98,468	139,724

Notes: Scenario 1 simulates a homogeneous patient population. Scenario 2 accounts for dose increases. In scenario 3, patients with HAQ scores 2.0 and higher pay costs associated with major surgery (mean cost of $31,861). Patients in scenario 4 have a mean baseline HAQ score of 1.0. 95% credible intervals are in parentheses.

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